

AMENDMENTS TO THE CLAIMS

1.-25. (Canceled)

26. (Currently amended) A genetically modified mouse whose genome comprises a homozygous disruption of the endogenous Shp2 gene in ~~at least a portion of~~ only neuronal forebrain cells of said mouse such that no Shp2 is expressed in said ~~portion of~~ neuronal forebrain cells, ~~wherein cells outside of the forebrain do not have a homozygous disruption of the endogenous Shp2 gene, and~~ wherein said genetically modified mouse exhibits an increased body weight in comparison to a mouse whose genome does not comprise said disrupted Shp2 gene in said ~~portion of~~ neuronal forebrain cells.

27. (Canceled)

28. (Previously presented) The genetically modified mouse of Claim 26, wherein said mouse has early-onset obesity.

29. (Previously presented) The genetically modified mouse of Claim 26, wherein said mouse has a resistance to leptin in comparison to a wild-type mouse.

30. (Previously presented) The genetically modified mouse of Claim 26, wherein the Shp2 protein level is decreased by 50-70% in a forebrain lysate of said mouse in comparison to a wild-type mouse.

31. (Previously presented) The genetically modified mouse of Claim 26, wherein triglyceride levels are increased in the serum of said mouse in comparison to a wild-type mouse.

32-43. (Canceled)

44. (Previously presented) The genetically modified mouse of Claim 26, wherein insulin levels are increased in the serum of said mouse in comparison to a wild-type mouse.

45. (Previously presented) The genetically modified mouse of Claim 26, wherein the homozygous disruption of the endogenous Shp2 gene comprises a deletion of exon 4.

46-52. (Canceled)

53. (Previously presented) A genetically modified mouse exhibiting an increased body weight in comparison to a wild-type mouse, wherein the genome of the calcium/calmodulin-dependent protein kinase II alpha (CamK2a)-expressing cells in the forebrain of the genetically modified mouse has been altered to lack expression of the endogenous Shp2 gene such that no Shp2 is expressed in the CamK2a-expressing forebrain cells, and wherein the genetically modified

mouse exhibits an increased body weight in comparison to a mouse that expresses the endogenous Shp2 gene in CamK2a-expressing forebrain cells.

54. (Previously presented) The genetically modified mouse of Claim 53, wherein the mouse has early-onset obesity.

55. (Previously presented) The genetically modified mouse of Claim 53, wherein the mouse has a resistance to leptin in comparison to a wild-type mouse.

56. (Previously presented) The genetically modified mouse of Claim 53, wherein triglyceride levels are increased in the serum of the mouse in comparison to a wild-type mouse.

57. (Previously presented) The genetically modified mouse of Claim 53, wherein insulin levels are increased in the serum of the mouse in comparison to a wild-type mouse.

58. (Previously presented) The genetically modified mouse of Claim 53, wherein the genetic alteration comprises a Cre-loxP-mediated truncation of the Shp2 gene.

59. (Previously presented) The genetically modified mouse of Claim 53, wherein the genetic alteration comprises a deletion of exon 4 in the endogenous Shp2 gene.